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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/072,010	10/25/2001	Jonathan W. Nyce	EPI-00312	5176
21971	7590	12/14/2004	EXAMINER	
WILSON SONSINI GOODRICH & ROSATI			JIANG, SHAOJIA A	
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PALO ALTO, CA 943041050			PAPER NUMBER	
			1617	
DATE MAILED: 12/14/2004				

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/072,010

Applicant(s)

NYCE, JONATHAN W.

Examiner

Shaojia A. Jiang

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 September 2004.
- 2a) ☒ This action is FINAL. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 160-162, 165 and 187-190 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 160-162, 165 and 187-190 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

This Office Action is a response to Applicant's amendment and response filed September 9, 2004 wherein claims 160-162, 165 have been amended; claims 163-164, and 166-186 are cancelled; claims 187-190 are newly submitted. Claims 1-159 are cancelled previously.

Currently, claims 160-162, 165 and 187-190 are pending in this application.

Claims 160-162, 165 and 187-190 are examined on the merits herein.

Applicant's amendment amending claims 160 and 165, filed September 9, 2004 with respect to the rejection made under 35 U.S.C. 112 first paragraph for lack of scope of enablement of record stated in the Office Action dated March 9, 2004 has been fully considered and is found persuasive to overcome the rejection since the recitations "prophylaxis" and "prevent or counter" have been removed from the claims. Therefore, the said rejection is withdrawn.

Applicant's amendment amending claim 165, filed September 9, 2004 with respect to the rejection made under 35 U.S.C. 112 second paragraph for lack of scope of enablement of record stated in the Office Action dated March 9, 2004 has been fully considered and is found persuasive to overcome the rejection since the recitation "the subject's tissue" has been removed from the claims. Therefore, the said rejection is withdrawn.

The following is new rejection(s) necessitated by Applicant's amendment filed on September 9, 2004.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 160-162, 165 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant's amendment filed September 9, 2004 with respect to amended claims herein has been fully considered but is deemed to insert new matter into the claims since the specification as originally filed does not provide support for "less than about 5 μ m" which read literally on from zero to about 5 μ m, **without lower limit**. The original specification merely discloses the ranges of particle size (see page 14 of the specification).

Consequently, there is nothing within the instant specification which would lead the artisan in the field to believe that Applicant was in possession of the invention as it is now claimed. See *Vas-Cath Inc. v. Mahurkar*, 19 USPQ 2d 1111, CAFC 1991, see also *In re Winkhaus*, 188 USPQ 129, CCPA 1975.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 160-162, 165 and 187-190 are rejected under 35 U.S.C. 103(a) as being unpatentable over Prendergast (4,956,355 of record) in view of Lieberman et al. (Pharmaceutical Dosage Forms, page 110).

Prendergast discloses that particular dehydroepiandrosterones (DHEA) herein are useful in a pharmaceutical composition or a pharmaceutical formulation of enteral, parental, injectable, topical, inhalations or nasal inhalation administration (see col.5 lines 32-64, 49 and 63-64). See abstract, col.1 lines 36-57, col. 4-5 and claim 6. Prendergast also discloses the effective amounts of dehydroepiandrosterones in the composition and other agents and pharmaceutically acceptable excipients within the instant claim in the compositions therein (col.5).

Prendergast does not expressly disclose the particular ranges of particle size herein, less than about 5 μm or about 0.5-10 μm or about 10-500 μm in size.

Lieberman et al. teaches that a skilled artisan in pharmaceutical science would clearly know that the granulation, determination of size, or size reduction of a solid pharmaceutical formulation, e.g., in nasal inhalation formulation, have several benefits, for example, as taught in a text book "Pharmaceutical Dosage Forms" Tables, (Volume

2) Ed. by Herbert A. Lieberman, Leon Leachman, and Joseph B. Schwartz (1989) at page 110.

Moreover, suitable particle sizes for inhalation are generally known and available to one of ordinary skill in the art. For example, "Remington: The Science and Practice of Pharmacy", 20th Ed, by Alfonso R Gennaro, teaches that the optimum size for inhalations is known to be 0.5-0.7 μm into the pulmonary cavity (see page 735 the right column). The book "Pharmaceutical Dosage Forms and Drug Delivery System" by Ansel et al. 6th Ed, page 454-455, teaches that the fine particle size for inhalations is known to range 0.5-5 μm (see page 455, the left column).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to determine and granulate the dehydroepiandrosterones particles in range of size herein for nasal inhalation.

One having ordinary skill in the art at the time the invention was made would have been motivated to determine and granulate the dehydroepiandrosterones particles in range of size herein for nasal inhalation, since particular dehydroepiandrosterones (DHEA) herein are known to be in a pharmaceutical composition for inhalations or nasal inhalation administration based on Prendergast.

As discussed above, the optimum size for inhalations is known to be 0.5-0.7 μm into the pulmonary cavity according to "Remington: The Science and Practice of Pharmacy", and the fine particle size for inhalations is known to range 0.5-5 μm according to "Pharmaceutical Dosage Forms and Drug Delivery System". Thus, the dehydroepiandrosterones compositions of Prendergast for inhalations or nasal

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inhalation intrinsically comprise dehydroepiandrosterones particles having less than about 5 μm or about 0.5-10 μm or about 10-500 μm in size.

Moreover, the known teachings of these books clearly support the examiner's position that it is obvious to one of ordinary skill in the art that using conventional techniques to make inhalable, respirable or nasal formulation of the known active agents are considered well within the skill of artisan in pharmaceutical science, involving merely routine skill in the art, in addition to suitable particle sizes for nasal inhalation generally known and being available to one of ordinary skill in the art.

It has been held that it is within the skill in the art to select optimal parameters, such as amounts of ingredients, in a composition in order to achieve a beneficial effect. See *In re Boesch*, 205 USPQ 215 (CCPA 1980).

Thus the claimed invention as a whole is clearly prima facie obvious over the combined teachings of the prior art.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 160, 165 and 187-190 are rejected under 35 U.S.C. 103(a) as being unpatentable Nyce (5,527,789, of record) in view of Lieberman et al. (Pharmaceutical Dosage Forms, page 110).

Nyce discloses a pharmaceutical composition comprising the instant DHEA having the chemical formula (I) in a therapeutically effective amounts and the instant ubiquinone having the chemical formula (II) with n being from 1 to 12, 1 to 10, 6 to 10, or 10, in the therapeutically effective amounts, and a pharmaceutical carrier or diluent (see abstract, claims 13-19). Nyce also discloses the particular effective amounts of DHEA, i.e., 1-3600 mg/kg, 5-1800 mg/kg, or 20-100 mg/kg (see col.6 lines 6-7); and the particular effective amounts of ubiquinone, i.e., 1-1200 mg/kg, 30-600 mg/kg, or 50-150 mg/kg (see col.5 lines 64-66), within the instant claimed range, about 0.1-49% or about 1-20% w/w, since converting the known actual amount by actual weight to weight percentage in a composition, w/w, is considered well within conventional skills in pharmaceutical science, involving merely routine skill in the art. The pharmaceutical composition of Nyce further comprises a preservative, an antioxidant, a flavoring agent (e.g., sugar, see col.7 line 10), a buffering agent, a dispersant, or a surfactant (see col.6 line 67 to col.8 line 1, and col.7 lines 33-38) an inert base, glycerol (glycerin, see col.7 line 11-12). Nyce also discloses the instant forms of the formulation, e.g., nasal spray (see col.7 line 17) oral, rectal, topical, transdermal, nasal, or parenteral including injectable (see col.5 lines 37-41, col.6 lines 40-67), in a solution (an aqueous liquor), suspension.

The cited prior art does not expressly disclose the particular particles of the active agents having size herein, less than about 5 μm or about 0.5-10 μm or about 10-500 μm in size.

Lieberman et al. teaches that a skilled artisan in pharmaceutical science would clearly know that the granulation, determination of size, or size reduction of a solid pharmaceutical formulation, e.g., in nasal inhalation formulation, have several benefits, for example, as taught in a text book "Pharmaceutical Dosage Forms" Tables, (Volume 2) Ed. by Herbert A. Lieberman, Leon Leachman, and Joseph B. Schwartz (1989) at page 110.

Moreover, suitable particle sizes for inhalation are generally known and available to one of ordinary skill in the art. For example, "Remington: The Science and Practice of Pharmacy", 20th Ed, by Alfonso R Gennaro, teaches that the optimum size for inhalations is known to be 0.5-0.7 μm into the pulmonary cavity (see page 735 the right column). The book "Pharmaceutical Dosage Forms and Drug Delivery System" by Ansel et al. 6th Ed, page 454-455, teaches that the fine particle size for inhalations is known to range 0.5-5 μm (see page 455, the left column).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to determine and granulate the dehydroepiandrosterones particles in range of size herein for nasal inhalation.

One having ordinary skill in the art at the time the invention was made would have been motivated to determine and granulate the dehydroepiandrosterones particles in range of size herein for nasal inhalation, since the nasal formulation or composition

comprising two instant active agents is known based on Nyce. According to conventional techniques to make inhalable, respirable or nasal formulation of the known active agents are considered well within the skill of artisan in pharmaceutical science, involving merely routine skill in the art, in addition to suitable particle sizes for nasal inhalation generally known and being available to one of ordinary skill in the art.

The known teachings of these books clearly support the examiner's position that it is obvious to one of ordinary skill in the art that using conventional techniques to make inhalable, respirable or nasal formulation of the known active agents are considered well within the skill of artisan in pharmaceutical science, involving merely routine skill in the art, in addition to suitable particle sizes for nasal inhalation generally known and being available to one of ordinary skill in the art.

It has been held that it is within the skill in the art to select optimal parameters, such as amounts of ingredients, in a composition in order to achieve a beneficial effect. See *In re Boesch*, 205 USPQ 215 (CCPA 1980).

Thus the claimed invention as a whole is clearly prima facie obvious over the combined teachings of the prior art.

Applicant is further requested to note that it is well settled that "intended use" of a composition or product, will not further limit claims drawn to a composition or product. See, e.g., *Ex parte Masham*, 2 USPQ2d 1647 (1987) and *In re Hack* 114, USPQ 161.

Applicant's remarks filed September 9, 2004 with respect to the rejections made under 35 U.S.C. 103(a) of record in the previous Office Action have been fully

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considered but are not deemed persuasive as to the nonobviousness of the claimed invention over the prior art. These remarks are believed to be adequately addressed by the obvious rejection presented above.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 165 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 13-19 of U.S. Patent No. 5,527,789 (of record).

Although the conflicting claims are not identical, they are not patentably distinct from each other because the patent are drawn to a pharmaceutical composition comprising the dehydroepiandrosterone and ubiquinone with n being from 1 to 10, 6 to 10, or 10, and pharmaceutically acceptable carrier such as an aqueous or a solid carrier. The claim of the instant application is drawn to a pharmaceutical composition or formulation, or kit comprising the same dehydroepiandrosterone and ubiquinone with n being from 1 to 12, 1 to 10, 6 to 10, or 10, in the effective amounts, and

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pharmaceutically acceptable carrier such as an aqueous or a solid carrier, and this pharmaceutical composition or formulation, or kit may be further comprises other agents such as preservatives, antioxidants flavoring agents, volatile oils, buffering agents, dispersants or surfactants.

In regard to the size of particles recited herein, as discussed above, 5,527,789 does teach various routes of administration, e.g., nasal spray (see col.7 line 17) oral, rectal, topical, transdermal, nasal, or parenteral including injectable (see col.5 lines 37-41, col.6 lines 40-67), in a solution (an aqueous liquor), suspension.

It is obvious to one of ordinary skill in the art that using conventional techniques to make inhalable, respirable or nasal formulation of the known active agents are considered well within the skill of artisan in pharmaceutical science, involving merely routine skill in the art, in addition to suitable particle sizes for nasal inhalation generally known and being available to one of ordinary skill in the art.

Therefore, the claimed invention in claim 165 is clearly seen to be obvious over claims 13-19 of U.S. Patent No. 5,527,789. Thus, Applicant's remarks are not found convincing as discussed above.

In view of the rejections to the pending claims set forth above, no claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Jiang, whose telephone number is (571)272-0627. The examiner can normally be reached on Monday-Friday from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, Ph.D., can be reached on (571)272-0629. The fax phone number for the organization where this application or proceeding is assigned is 703.872.9307.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



S. Anna Jiang, Ph.D.
Primary Examiner, AU 1617
December 3, 2004